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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/879,320	06/12/2001	Ajay Hasmukhlal Upadhyay	RD 01022	5176

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EXAMINER	
CHANNAVAJJALA, LAKSHMI SARADA	
ART UNIT	PAPER NUMBER
1611	
MAIL DATE	DELIVERY MODE
08/06/2009	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	09/879,320	UPADHYAY, AJAY HASMUKHLAL	
	Examiner	Art Unit	
	Lakshmi S. Channavajjala	1611	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *5-27-09*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *2-4,8,33,34 and 37* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *2, 3, 4, 8, 33, 34 and 37* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Receipt of RCE dated 5-27-09 and amendment and remarks dated 5-5-09 is acknowledged.

Continued Examination Under 37 CFR 1.114

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 5-27-09 has been entered.

Claims 2, 3, 4, 8, 33, 34 and 37 are pending. Claims 1, 5-7, 9-32 and 35-36 are canceled in the instant application.

The following NEW rejection is applied to the instant amended claims:

Claim Rejections - 35 USC § 103

2. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Claims 1-8 and 31-37 are rejected under 35 U.S.C. 103(a) as being unpatentable over US 6,372,252 to Blume et al (Blume) in view of US 5,032,406 to Dansereau et al (Dansereau), US 3,627,583 to Troy et al and US 6,623,756 to Wilber et al (Wilber) or US 6,372,252 to Blume et al (Blume) in view of US 5,032,406 to Dansereau et al (Dansereau) and US 6,623,756 to Wilber et al (Wilber .

Blume teaches immediate and sustained release formulations comprising guaifenesin. Blume teaches loading guaifenesin and methocel into a high shear mixer, mixed at high speed, adding water and further mixing at additional time to complete granulation. The composition is next dried in fluid dryer and then passed through a mill fitted a suitable size screen (col. 7, lines 63 through col. 8, lines 23). Thus, the resulting material of Blume reads on agglomerated mixture because the processing of the material involves the same steps as described in the instant application.

Blume fails to teach granulation of guaifenesin with polyvinylpyrrolidone.

Dansereau teaches a tablet composition that provides dual action, for immediate and sustained release, comprising an outer tablet and an inner tablet respectively. The active ingredient of both inner and outer tablets comprises guaifenesin. The inner tablet particularly comprises guaifenesin and polyvinylpyrrolidone (PVP) (example I). Dansereau teaches that the inner tablet is made as follows (col. 6):

The inner tablet is made by oscillating guaifenesin and half of the polyvinylpyrrolidone through a 30 mesh screen. The blend is then transferred to a pharmaceutical grade blender and mixed until it is of uniform consistency. It is then granulated with polyvinylpyrrolidone that had been previously dissolved in a sufficient amount of purified water to make a solution of from about 8% to about 12% of polyvinylpyrrolidone. This mixture is discharged and dried in a forced air oven at 40° C. until the water content is less than 1%. The dried granulation is then oscillated through a 12 mesh screen and returned to the blender. The remaining polyvinylpyrrolidone, microcrystalline cellulose and talc are added to this dried granulation and mixed until it is of uniform consistency. Finally, zinc stearate is added and the mixture is mixed until it is of uniform consistency. This mixture is then compressed into inner tablets using a standard tableting press.

Thus, the resulting inner tablet composition of Dansereau read on the claimed agglomerate mixture because the process involves the same steps as described in the instant specification (page 3, lines 15-20). Dansereau fails to teach the claimed particle sizes.

Wilber teaches tablets for controlled release of a desired drug that are directly compressed from a flowable, compressible mixture of the drug and a rheology modifying polymer or a copolymer and additional excipients (abstract). The rheology modifier is a homopolymer or copolymer is processed into a desirable granular size by compacting into large agglomerates or aggregates and subsequently fractured into smaller granules and screened to suitable particle size of low amounts of dust, such that the flow characteristics and compressibility are good and the tablets are directly

compressed (col. 4, L 44-48). Wilber teaches that the particle size of the granulated polymers is generally falls through 40-45 mesh but retained on 150 or 200 mesh (col. 4, l 44-67). When converted the 40-45 mesh equals 420 microns and 150-200 mesh size equals 75-100 microns. Thus the particle size ranges between 75-420 microns and overlaps with instant 45-425.Wilber also teaches that the over sized particles should be 5% or less and under sized particles should be 25% or less (lines bridging col. 4-5). Wilber teaches that the resulting optimum sized particles obtained are free flowing and are suitable for direct compression. The exemplified compositions of Wilber teach flow rates and compressibility values such as in examples 1-3. Wilber teaches a number of pharmaceutical agents that may be suitable for compressing in to tablets including guaifenesin (col. 6, L 54) but does exemplify guaifenesin.

Troy teaches tablets formed by direct compression from a mixture of an active material such as therapeutic material and as a direct compression vehicle dry, free-flowing, granular sugar and a binder (abstract). Troy teaches that in order to obtain free-flowing particles of 12 mesh to 325 mesh (col. 1, L 50-65). Troy states that tablets result in good physical properties and readily dissolve in aqueous media (col. 1 and col. 4, L 1-10). Troy suggests mixing sugar and the binder to effect agglomeration of about 325 mesh (44 microns according to the declaration submitted by applicants on 10-26-07) but not greater than 12 mesh (col. 3, L 7-15 and lines 46-61). Among the active agents, Troy suggests antitussives but does not explicitly state employing guaifenesin.

It would have been obvious for one of an ordinary skill in the art at the time of the instant invention from the teachings of Troy and Wilbur that particle sizes between 12-

325 or 20-200 respectively, are important for free flowing and the ability for compression such that the drug is released at a determined rate from the compressed tablet. Troy teaches that too fine a powder causes capping and while sizing of the granules particles is important for free flowing of drug. Wilbur suggests the allowed amounts of fines and oversized particle within which the tablets can be easily compressed. Troy as well as Dansereau recognizes PVP as a suitable binder for compressible tablets, particularly guaifenesin (Dansereau). Accordingly, it would have been obvious for one of an ordinary skill in the art at the time of the instant invention was made to employ PVP for the processing and preparation of compressible guaifenesin tablets of Blume because Troy as well as Dansereau recognize PVP as a suitable binder and Dansereau recognizes methylcellulose (Blume) and PVP as equivalent binders as well as disintegrants in preparing a sustained release compressible tablet preparation comprising guaifenesin.

With respect to the claimed particle sizes, Blume teaches that no more than 30% granulation material passes through 100 mesh (150 microns) and not more than 10% retained on 10-mesh screen (greater than 850 microns). Thus, majority of the particles of Blume are in the range of 150 microns – 2 mm and a smaller percentage of particles are below 150 microns. A maximum of 30% of the particles that pass through the 100-mesh screen, according to Blume, could be any size below 150 microns (as low as 45 microns claimed in the instant invention). While Blume does not teach the exact percentages of particle sizes claimed in the instant application, there is an overlap in the particle sizes between instant application and that of Blume (150 nm to 425 nm). On the

other hand, Wilbur suggests free flowing particles of appropriate size (not too fine a powder or not too oversized) are easy to compress and Troy suggests a particle size of 12 mesh (1.41 mm) to 325 mesh (44 microns) as suitable for free flowing, stable and compressible tablets. Accordingly, a skilled artisan would have readily optimized the particle sizes of the granulated PVP and guaifenesin between 12 mesh and 325 mesh sizes such that the particles have an optimum flow rate, strength and stability and yet do not show capping.

For the claimed additives such as glidants, lubricants, silica, stearic acid etc., Blume and Dansereau teach the conventional excipients including lubricants such as magnesium stearate, calcium stearate etc; binders such as povidone (polyvinylpyrrolidone), gelatin, starch; glidants such as talc or silicon dioxide, stabilizers and other excipients such as lactose, sorbitol etc. Accordingly, in the absence of evidence to the criticality of the specific excipients and their amounts (claims 3-4 & 33-34), it would have been obvious for one of an ordinary skill in the art at the time of the instant invention was made to the choose the appropriate excipient and optimize the amounts of the same in the composition of Blume with an expectation to obtain compressed tablets of desired compressibility or hardness and very less friability because the cited prior art desires the same features.

Response to Arguments

3. Applicant's arguments filed 5-5-09 have been fully considered but they are not persuasive.

4. Applicants state that during the interview dated April 28, 2009, applicant's representative pointed out that applicant can produce compressed dosage forms (tablets) from guaifenesin compositions under relatively low compressive forces to produce tablets that exhibit low friability, high hardness, and are resistant to capping, citing the last paragraph of the specification. Applicanst state that it was agreed that if applicant amended claim 37 to specify "tablet", as well as a numerical range of "tablet hardness" in place of the phrase "high hardness", that claim 37, and claims dependent thereon would be allowable.

5. However, the interview summary dated 4-28-09 does not state that the claims will be allowable upon amending the claims to recite the above features. Examiner clearly stated that the limitations will be considered. Upon consideration and further search, new art has been identified that teaches compressible tablets produced from free flowing, low friability and high compressibility particles (Wilbur), which according to the examiner is pertinent to the instant invention. Hence a new ground of rejection has been made. The newly cited art provides a rationale for choosing the appropriate particle size of the granular material to be compressed and is hence applied as prior art. With respect to the low friability and high hardness of the instant examples, Wilbur suggests these features in preparing compressed tablets.

6. With respect to the results in tables 2A-2G, it is observed that while compositions of the instant invention do not exhibit capping at any compression force applied, comparative examples 1 and 3 also do not exhibit capping at the highest compression force. For the friability, comparative examples do provide low friability (<1%0 even at

highest force applied. Thus, it is not clear if the instant compositions provide any unexpected advantage over the comparative compositions.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Lakshmi S. Channavajjala whose telephone number is 571-272-0591. The examiner can normally be reached on 9.00 AM -5.30 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Sharmila G. Landau can be reached on 571-272-0614. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Lakshmi S Channavajjala/
Primary Examiner, Art Unit 1611

August 3, 2009